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Amendments to the Specification

Please amend paragraph 0012 as follows:

[0012] The cytokines of the IL-1-family, including IL-18, possess a variety of inflammatory and immunoregulatory properties during the first line and secondary response to infection (Dinarello 1996 and Nakanishi 2001). Six new members of the interleukin-1 (IL-1) gene family have been discovered from expressed sequence tag data base searches (Barton 2000, Busfield 2000, Debets 2001, Kumar 2000, Lin 2001, Mulero 1999, Pan 2001 and Smith 2000). These proteins share a common β -barrel pattern consisting of 12 β -strands and significant amino acid homology with the IL-1 receptor antagonist (IL-1Ra), IL-1 β and IL-18. These new members of the IL-1 family are derived from a common ancestor as are IL-1 and IL-18 (Nicklin 2002, Taylor 2002). Except for IL-18, each maps to the same region on human chromosome 2 (Nicklin 2002, Mulero 2000, Taylor 2002 and Busfield 2000). Their biological function of these IL-1 homologues is presently unknown. Five different splice variants of the novel IL-1 homologue IL-1H4 (IL-1F7a-e) have been described (Busfield 2000, Kumar 2000, Pan 2001, Smith 2000, Taylor 2002). The first isoform described, IL-1F7a, has an unique N-terminus consisting of exon 3 of the IL-1 F7 gene, which is not present in the other splice variants of the gene. The short isoforms IL-1F7c, IL-1F7d and IL-1F7e lack exon 4, 2 or both, respectively. Only IL-1F7b and c containing exon 1 and 2 express a N-terminal prodomain that has a potential caspase-1 (ICE) cleavage site(s) (Kumar 2002). In addition to these splice variants, amino acid polymorphisms (V31 G and A42T) exist in IL-1F7b based on two base pair mutations in exon 2 (Kumar 2000, Pan 2001). Despite extensive data base searches and sequencing of the IL-1-gene locus, no murine homologue of IL-1 H4 has yet been found. IL-1F7b shares significant sequence homology with IL-18. The hallmark for IL-18 activity is its ability to induce IFN γ in T-cells or natural killer (NK) cells in the presence of IL-2, IL-12 or IL-15 as costimulant. The activity of IL-18 is mediated via the IL-18R complex consisting of the ligand-binding chain termed IL-18R.alpha. (Torigoe 1997) and a signaling chain termed IL-18 β (3 (Born 1998, Kim 2001). Upon binding to the IL-18R α chain and formation of the hetero complex with the IL-18R β chain, IL-18 induces activation of IL-1 receptor-associated kinase and TNF receptor-associated factor 6 (TRAF-6). These activated kinases eventually result in the translocation of nuclear factor κ -B (NF- κ B)

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(Matsumoto, Robinson). IL-1F7b has been reported to bind to the IL-18R.alpha. using a receptor pulldown assay (Pan 2001) or computerchip-based binding studies (~~BiaCore~~ BIACORE®) (Mulero 2000). Significant but low affinity binding of $K_d=130$ mM was only observed for the mature form of IL-1F7b without the propeptide suggesting biological relevance to IL-1F7b processing by ICE (Kumar 2002). Despite the binding to the IL-18R α , no IL-18-like or antagonistic activity of either pro or mature IL-1F7b was demonstrated (Pan 2001, Kumar 2002).

Please amend paragraph 0073 as follows:

[0073] Human IL-18 (accession no. D49950) and human IL-1F7b (accession no. AF200496) are shown. Alignment was generated using Expert Protein Analysis System (~~Expasy~~ EXPASY®) with additional manual adjustment. The amino acid identity of IL-18 with IL-1F7b is 28% and the similarity 55%. The underlined amino acids represent the ICE-cleavage site in IL-18 and the predicted cleavage site in IL-1F7b.

Please amend paragraph 00135 as follows:

[0135] The following oligonucleotide primers were used to clone the IL-1F7b cDNA from a human spleen library (~~Clontech~~ CLONTECH® HLOOIB, BD Biosciences ~~Clontech~~ CLONTECH, Palo Alto, Calif.): sense primer 5'GTTGAGTAATAAACTCAACG (SEQ ID NO: 1), reverse primer 5'GTTCAATGGGGCAGTTTC (SEQ ID NO: 2) (specific for clone AF200496 (~~GenBank~~ GENBANK®) (Kumar 2000). The IL-1F7b cDNA was reamplified using a second pair of primers introducing cleavage sites for EcoRI at the 5' and XbaI at the 3' end (sense primer 5'-ATATGAATTCATGTCCTTGTGGGGGAG (SEQ ID NO: 3); reverse primer 5'-TATATCTAGAAGTTTCCTAATCGCTGACC (SEQ ID NO: 4). Using TA-cloning the IL-1F7b cDNA was transferred into pGEM-T Easy® (Promega Corp. Madison, Wis.) according to the manufacturer's instructions and the correct sequence was verified. The IL-1F7b. cDNA was then ligated into pPROEXTMHTa (~~Gibco~~ GIBCO-BRL) for bacterial expression using the EcoRI and XbaI site. The pPROEXTMHTa vector contains a N-terminal Hisx6 tag for affinity purification of the expressed protein. The pPROEXTMHTa/IL-1F7b plasmid was transformed into the competent E. coli strain DH5a (~~Gibco~~ GIBCO-BRL). An overnight culture (10 ml) was

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added to 200 ml of LB medium containing 100 µg/ml ampicillin and grown until a density of 0.6-1 OD₆₀₀.

Please amend paragraph 0139 as follows:

[0139] PBMC were either purified from platelet-depleted residual leukocytes or from heparinized blood of healthy donors. Platelet-depleted leukocytes or whole blood was diluted 1:1 with saline and applied to ~~Ficoll-Histopaque~~ FICOLL-HISTOPAQUE® gradients (Sigma) as described previously (Kim 2001). After centrifugation, the cells from the interface were harvested, washed three times in saline and resuspended in RPMI. The isolated PBMC were kept on ice until the assay was started.

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